

Applicants respectfully request reconsideration of pending claims 1-31 and 42-45.

I. Rejection Under 35 U.S.C. § 112, Second Paragraph

Claim 43 has been rejected under 35 U.S.C § 112, second paragraph, as allegedly being indefinite (Office Action, paragraph 2). The Examiner opines that it is unclear which two different oligonucleotides claim 43 refers to.

Solely in an effort to advance prosecution of this application, Applicants have amended claim 43 to recite a pharmaceutical composition comprising at least two synthetic oligonucleotides according to claim 2 in a pharmacologically acceptable carrier, wherein the at least two synthetic oligonucleotides are different. No new matter has been added by way of this amendment.

Applicants submit that claim 43, as amended, satisfies the requirements of 35 C.F.R. § 112, second paragraph. Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

II. Rejection Under 35 U.S.C. § 102(e).

Claims 1 and 44 have been rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by Cha *et al.* (U.S. Patent No. 6,071,693) ("Cha") (Office Action, paragraph 4). This ground of rejection is respectfully traversed.

SEQ ID NO:126 disclosed in Cha does not anticipate claim 1. SEQ ID NO:126 disclosed in Cha is only partially identical to SEQ ID NO:117. Further, claim 1 encompasses an oligonucleotide having the nucleotide sequence of SEQ ID NO:117, as set forth in Table 1A.

Similarly, claim 44 recites a pharmaceutical composition comprising at least one oligonucleotide of claim 1. Table 1A shows various modifications to SEQ ID NO:117. Specifically, Table 1A shows the following sequences: TT*CGCGACCCAACACTACTC (HCV-242), TTCG*CGACCCAACACTACTC (HCV-243), and TT*CG*CGACCCAACACTACTC (HCV-242), wherein *C represents 5-methyl-2'deoxyctidine (see last column in Table 1A, page 24). In contrast, Cha discloses a DNA sequence, which comprises SEQ ID NO:122, but which does not disclose the modified form SEQ ID NO:117 that is set forth in Table 1A, and which is encompassed by claim 1.

Thus, Applicants submit that claims 1 and 44 are not anticipated by Cha, and satisfy all the requirements of 35 U.S.C. § 102(e). Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

III. Rejection Under 35 U.S.C. § 103(a)

Several rejections under 35 U.S.C. § 103 have been made (Office Action, paragraphs 6-8). In order to respond completely and accurately, Applicants will address each ground separately below.

A. Hogan *et al.* and Maertens *et al.*

Claims 2-6, 8-20, 25, 27, 28, 30, and 43 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hogan *et al.*, USPN 5,424,413 ("Hogan") and Maertens *et al.*, USPN 5,846,704 ("Maertens") (Office Action, paragraph 6). This ground of rejection is respectfully traversed.

Hogan discloses a nucleic acid probe having at least one nucleic acid strand, which has two separate target-specific regions that hybridize to a target nucleic acid. However, the Hogan probes bind contiguous regions on the target nucleic acid, whereas the oligonucleotides encompassed by the instant claims bind at least two non-contiguous regions on the target nucleic acid (see independent claim 2, from which the other rejected claims depend). The Examiner cites Figure 4A in Hogan, to support the contention that these probes render the instant claims obvious. However, as shown in Figure 5A, it is clear that these probes target contiguous regions on the target nucleic acid. Figure 5A is stated to be an "example of the general structure shown in Figure 4" (Hogan, Column 13, line 51). Nowhere does Hogan suggest the use of synthetic oligonucleotides comprising a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA.

The Hogan patent also does not disclose an HCV messenger or genomic RNA, as was acknowledged by the Examiner. Further, Hogan does not teach or suggest the use of synthetic oligonucleotides comprising a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic DNA

To supply the deficiency in Hogan, the Examiner cites Maertens. The probes in Maertens target contiguous sequences from the 5' untranslated regions of HCV. In contrast, the oligonucleotides encompassed by the instant claims comprise a sequence complementary to at least two non-contiguous regions of HCV messenger or genomic RNA (see independent claim 2, from which the other rejected claims depend). Thus, the probes disclosed in Maertens do nothing to supply the deficiency of Hogan. Furthermore, Maertens, either alone or in combination with Hogan, does not teach or suggest the use of synthetic oligonucleotides

comprising a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic DNA.

Thus, Applicants submit that independent claim 2 is non-obvious in view of the teachings of Hogan and Maertens. Similarly, claims 3-6, 8-20, 25, 27, 28, 30 and 43, wherein they depend directly or indirectly upon independent claim 2, and thus contain all the limitations thereof, also satisfy the requirements of 35 U.S.C. § 103(a).

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

B. Hogan et al., Maertens et al., and Seki et al.

Claims 7, 31, 43 and 45 have been rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Hogan, in view of Maertens, and in further view of Seki et al. (CA 2104649) ("Seki") (Office Action, paragraph 7).

This ground of rejection is respectfully traversed.

"To establish a *prima facie* case of obviousness based on a combination of the content of various references, there must be some teaching, suggestion or motivation in the prior art to make the specific combination that was made by the applicant." *In re Dance*, 160 F.3d 1339, 1343, 48 USPQ2d 1635, 1637 (Fed. Cir. 1998); *see also In re Dembiczak*, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) ("Our case law makes clear that the best defense against the subtle but powerful attraction of a hindsight-based obviousness analysis is rigorous application of the requirement for a showing of the teaching or motivation to combine prior art references."); *In re Fritch*, 23 USPQ2d 1780, 1784 (Fed. Cir. 1992) (modification of the

teachings of a prior art reference is not established by the teachings of a second prior art reference "*unless the prior art suggests the desirability of the modification*" (emphasis added)). Applicants submit that the motivation to combine the cited references is completely lacking.

Hogan and Maertens are discussed in detail elsewhere herein.

With respect to claim 7, the fact that Seki discloses SEQ ID NO:6, which is only partially identical to SEQ ID NO:47, does not render claim 7 obvious over the combined cited references, does not supply the deficiencies of Hogan and Maertens. Claim 7 is dependent on claim 2, and thus, incorporates all the limitations thereof. Thus, claim 7 requires (1) that the oligonucleotide comprises a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA (see claim 2), and (2) that one portion of the oligonucleotide has the sequence SEQ ID NO:47 (see claim 7). SEQ ID NO:47 is a single sequence, which is specific for only one region of an HCV messenger or genomic RNA. It does not comprise another sequence portion complementary to at least one other non-contiguous region of an HCV messenger or genomic RNA, as required by claim 7, wherein it depends on independent claim 2. Furthermore, Seki does not disclose or suggest an oligonucleotide according claim 2 (which comprises a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA), wherein one portion of the oligonucleotide has the sequence SEQ ID NO:47. Instead, Seki merely discloses a sequence that may comprise one portion of an oligonucleotide that is complementary to at least two non-contiguous regions of the HCV messenger or genomic RNA.

With respect to claim 31, the fact that Seki discloses SEQ ID NO:229, which is only partially identical to SEQ ID NO:160, does render claim 31 obvious over the combined cited references, and does not supply the deficiencies of Hogan and Maertens. Claim 31 is dependent on claim 30, which in turn is dependent on claim 8, which in turn is multiply dependent on independent claims 1 or 2. For the reasons set forth above, neither Hogan nor Maertens disclose or suggest a synthetic oligonucleotide comprising a sequence complementary to at least two non-contiguous regions of an HCV messenger or genomic RNA, as is required by independent claim 2. Based on its dependency, claim 31 is not directed solely to an oligonucleotide having the nucleotide sequence of SEQ ID NO:160. Instead, claim 31 is directed to an oligonucleotide having the nucleotide sequence of SEQ ID NO:160, which is modified by incorporating at least one additional triplex forming strand (see claim 30).

Similarly, claims 43 and 45, which are pharmaceutical composition claims, are also not obvious over Hogan, Maertens or Seki for the same reasons outlined above with respect to claims 7 and 31.

Thus, neither Hogan, Maertens or Seki, alone or in combination, discloses or suggests the claimed oligonucleotides of claims 7 and 31 or the claimed pharmaceutical compositions of claims 43 and 45.

Applicants submit that claims 7, 31, 43 and 45 are non-obvious in view of the combined teachings of Hogan, Maertens, and Seki, and satisfy all the requirements of 35 U.S.C. § 103(a). Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

C. Hogan et al., Maertens et al., and Cha et al.

Claims 21 and 29 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Hogan, in view of Maertens, and further in view of Cha *et al.* (U.S. Patent No. 6,071,693) ("Cha") (Office Action, paragraph 8).

This ground of rejection is respectfully traversed.

Hogan and Maertens are discussed in detail elsewhere herein.

With respect to claim 21, the fact that Cha discloses SEQ ID NO:126, which is only partially identical to SEQ ID NO:122, does not render claim 21 obvious over the combined cited references, and does not supply the deficiencies of Hogan and Maertens. Claim 21 is directed to an oligonucleotide having the nucleotide sequence SEQ ID NO:122, as set forth in Table 1A. Table 1A shows various non-obvious modifications to SEQ ID NO:122. Specifically, Table 1A shows the following RNA sequence: uucgcgaccCAacacuacuc, wherein lower case letters represent 2'-O-methyl ribonucleotides and upper case letters represent deoxyribonucleotides (see footnote in Table 1A, page 25). In contrast, Cha discloses a DNA sequence, which comprises SEQ ID NO:122, but which does not disclose or suggest the modified form SEQ ID NO:122 that is set forth in Table 1A, and which is encompassed by claim 21. Moreover, none of Hogan, Maertens or Cha, either alone or in combination, discloses or suggests such an oligonucleotide.

With respect to claim 29, SEQ ID NO:126 disclosed in Cha does not render claim 29 obvious either alone or in combination with Hogan and Maertens. SEQ ID NO:126 disclosed in Cha is only partially identical to SEQ ID NO:117. Further, claim 29 encompasses an oligonucleotide having the nucleotide sequence of SEQ ID NO:117, as set forth in Table 1A.

Table 1A shows various modifications to SEQ ID NO:117. Specifically, Table 1A shows the following sequences: TT*CGCGACCCAACACTACTC (HCV-242), TTCG*CGACCCAACACTACTC (HCV-243), and TT*CG*CGACCCAACACTACTC (HCV-242), wherein *C represents 5-methyl-2'deoxyctidine (see last column in Table 1A, page 24). In contrast, Cha discloses a DNA sequence, which comprises SEQ ID NO:117, but which does not disclose the modified form SEQ ID NO:117 that is set forth in Table 1A, and which is encompassed by claim 29. Moreover, none of Hogan, Maertens or Cha, either alone or in combination, discloses or suggests such an oligonucleotide.

Thus, Applicants submit that claims 21 and 29, are non-obvious in view of the teachings of Hogan, in view of Maertens, and further in view of Cha, and satisfy all the requirements of 35 U.S.C. § 103(a).

Accordingly, reconsideration and withdrawal of this rejection is respectfully requested.

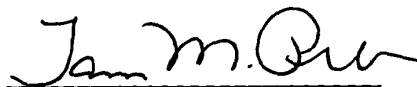
IV. Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully submit that this application is now in condition for allowance. If a telephone interview would advance prosecution of the application, the Examiner is invited to call the undersigned at the number listed below.

Applicants are submitting this Amendment within three months of the Office Action dated 05 June 2002. Thus, no fees are due in connection with this Amendment. However, if there are any other fees due in connection with the filing of the response, please charge the fees

to Deposit Account 08-0219. Also, please charge any fees underpaid or credit any fees overpaid to the same Deposit Account.

Respectfully submitted,



Tamera M. Pertmer, Ph.D.
Agent for Applicant
Registration No. 47,856

Date: 05 Sept. 2002
HALE AND DORR LLP
60 State Street
Boston, MA 02109
Tel: (617) 526-6000
Fax: (617) 526-5000